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(54) **DETECTION OF METHICILLIN-RESISTANT STAPHYLOCOCCUS AUREUS**

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See application file for complete search history.

(56) **References Cited**

**U.S. PATENT DOCUMENTS**

5,702,895 A \* 12/1997 Matsunaga et al. .... 435/6  
6,156,507 A 12/2000 Hiramatsu et al.  
6,379,897 B1 4/2002 Weidenhammer et al.  
7,449,289 B2 11/2008 Huletsky et al.  
7,888,075 B2 2/2011 McCarthy et al.  
2004/0076990 A1 4/2004 Picard et al.  
2005/0019893 A1 1/2005 Huletsky et al.  
2006/0057613 A1 3/2006 Ramakrishnan et al.  
2007/0054296 A1 3/2007 Piepenburg et al.  
2007/0082340 A1 4/2007 Huletsky et al.  
2008/0227087 A1 9/2008 Huletsky et al.  
2009/0081663 A1 3/2009 Paitan

**FOREIGN PATENT DOCUMENTS**

EP 0887424 A2 12/1998  
EP 1 529 847 B1 4/2006  
WO WO 97/31125 A2 8/1997  
WO WO 02/099034 A2 12/2002  
WO WO 2006/111028 A1 10/2006  
WO WO 2008/080620 7/2008  
WO WO 2008/129428 A2 10/2008  
WO WO 2009/018000 A1 2/2009  
WO WO 2009/090310 A1 7/2009

**OTHER PUBLICATIONS**

Lowe et al. Nucleic acid research, 1990, vol. 18(7), p. 1757-1761.\*  
Donnio et al., “Partial Excision of the Chromosomal Cassette Containing the Methicillin Resistance Determinant Results in Methicillin-Susceptible *Staphylococcus aureus*,” J. Clin. Microbiol. 43(8):4191-4193 (2005).

International Search Report and Written Opinion, PCT/US08/13922, mailed Aug. 5, 2009.

Bishop et al., “Concurrent Analysis of Nose and Groin Swab Specimens by the IDI-MRSA PCR Assay Is Comparable to Analysis by Individual-Specimen PCR and Routine Culture Assays for Detection of Colonization by Methicillin-Resistant *Staphylococcus aureus*,” J. Clin. Microbiol. 44(8):2904-2908 (2006).

Brown et al., “Real-Time PCR Detection of *S. aureus* and MRSA from Wound, Fluid and Respiratory Samples,” Abstract No. C-077. American Society for Microbiology Conference, Orlando, Florida, May 21-25, 2006.

Desjardins et al., “Evaluation of the IDI-MRSA Assay for Detection of Methicillin-Resistant *Staphylococcus aureus* from Nasal and Rectal Specimens Pooled in a Selective Broth,” J. Clin. Microbiol. 44(4):1219-1223 (2006).

Drews, et al., “Verification of the IDI-MRSA Assay for Detecting Methicillin-Resistant *Staphylococcus aureus* in Diverse Specimen Types in a Core Clinical Laboratory Setting,” J. Clin. Microbiol. 44(10):3794-3796 (2006).

Huletsky et al., New Real-Time PCR Assay for Rapid Detection of Methicillin-Resistant *Staphylococcus aureus* Directly from Specimens Containing a Mixture of Staphylococci, J. Clin. Microbiol. 42(5):1875-1884 (2004).

Rupp et al., “Be Aware of the Possibility of False-Positive Results in Single-Locus PCR Assays for Methicillin-Resistant *Staphylococcus aureus*,” J. Clin. Microbiol. 4(6):2317 (2006).

Warren et al., “Detection of Methicillin-Resistant *Staphylococcus aureus* Directly from Nasal Swab Specimens by a Real-Time PCR Assay,” J. Clin. Microbiol. 42(12):5578-5581. (2004).

Cuny et al., “PCR for the identification of methicillin-resistant *Staphylococcus aureus* (MRSA) strains using a single primer pair specific for *SCCmec* elements and the neighbouring chromosome-borne *orfX*,” Clin. Microbiol. Infect. 11:834-837 (2005).

Hagen et al., “Development of a real-time PCR assay for rapid identification of methicillin-resistant *Staphylococcus aureus* from clinical Samples,” Int. J. Med. Microbiol. 295:77-86.

Holfelder et al., “Direct detection of methicillin-resistant *Staphylococcus aureus* in clinical specimens by a nucleic acid-based hybridisation assay,” Clin. Microbiol. Infect. 12:1168-1167 (2006).

Huletsky et al., “Identification of methicillin-resistant *Staphylococcus aureus* carriage in less than 1 hour during a hospital surveillance program,” Clin. Infect. Dis. 40:976-981 (2005).

Zhang et al., “Novel multiplex PCR assay for characterization and concomitant subtyping of staphylococcal cassette chromosome *mec* types I to V in methicillin-resistant *Staphylococcus aureus*,” J. Clin. Microbiol. 43:5026-5033 (2005).

European Application No. 08868000.4, filed Dec. 19, 2008; extended European search report mailed Feb. 28, 2011.

European Application No. 08868000.4, filed Dec. 19, 2008; office action mailed Jan. 13, 2012.

Chinese Patent Application No. 200880123825.5, Filed: Dec. 19, 2008; office action mailed Jun. 5, 2012.

Israeli Patent Application No. 206499; Filed: Dec. 19, 2008; office action mailed Mar. 5, 2012.

\* cited by examiner

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(57) **ABSTRACT**

The present invention provides improved tests for the detection of methicillin-resistant *Staphylococcus aureus*. The tests are particularly useful for eliminating false positive results due to the presence of a mixed bacterial population in patient samples.